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Document Processing Center (TS-790)
Office of Pollution Prevention and Toxics
Environmental Protection Agency
401 M Street., S.W.
Washington, D.C. 20460
Attn: Section 8(e) Coordinator (CAP Agreement)

Dear Coordinator:

8ECAP-0025

On behalf of the Regulatee and pursuant to Unit II B.1.b. and Unit II C of the 6/28/91CAP Agreement, E.I. Du Pont de Nemours and Co. hereby submits (*in triplicate*) the attached studies. Submission of this information is voluntary and is occasioned by unilateral changes in EPA's standard as to what EPA now considers as reportable information. Regulatee's submission of information is made solely in response to the new EPA §8(e) reporting standards and is not an admission: (1) of TSCA violation or liability; (2) that Regulatee's activities with the study compounds reasonably support a conclusion of substantial health or environmental risk or (3) that the studies themselves reasonably support a conclusion of substantial health or environmental risk.

The "Reporting Guide" creates new TSCA 8(e) reporting criteria which were not previously announced by EPA in its 1978 Statement of Interpretation and Enforcement Policy, 43 Fed Reg 11110 (March 16, 1978). The "Reporting Guide states criteria which expands upon and conflicts with the 1978 Statement of Interpretation. Absent amendment of the Statement of Interpretation, the informal issuance of the "Reporting Guide" raises significant due processes issues and clouds the appropriate reporting standard by which regulated persons can assure TSCA Section 8(e) compliance.

For Regulatee,

8E CAP

RECEIVED 4/24/95

Mark H. Christman
Counsel
Legal D-7158
1007 Market Street
Wilmington, DE 19898
(302) 774-6443

ATTACHMENT 1

Submission of information is made under the 6/28/91 CAP Agreement, Unit II. This submission is made voluntarily and is occasioned by recent changes in EPA's TSCA §8(e) reporting standard; such changes made, for the first time in 1991 and 1992 without prior notice and in violation of Regulatee's constitutional due process rights. Regulatee's submission of information under this changed standard is not a waiver of its due process rights; an admission of TSCA violation or liability, or an admission that Regulatee's activities with the study compounds reasonably support a conclusion of substantial risk to health or to the environment. Regulatee has historically relied in good faith upon the 1978 Statement of Interpretation and Enforcement Policy criteria for determining whether study information is reportable under TSCA §8(e), 43 Fed Reg 11110 (March 16, 1978). EPA has not, to date, amended this Statement of Interpretation.

After CAP registration, EPA provided the Regulatee the June 1, 1991 "TSCA Section 8(e) Reporting Guide". This "Guide" has been further amended by EPA, EPA letter, April 10, 1992. EPA has not indicated that the "Reporting Guide" or the April 1992 amendment supersedes the 1978 Statement of Interpretation. The "Reporting Guide" and April 1992 amendment substantively lowers the Statement of Interpretation 's TSCA §8(e) reporting standard[2]. This is particularly troublesome as the "Reporting Guide" states criteria, applied retroactively, which expands upon and conflicts with the Statement of Interpretation.[3] Absent amendment of the Statement of Interpretation, the informal issuance of the "Reporting Guide" and the April 1992 amendment clouds the appropriate standard by which regulated persons must assess information for purposes of TSCA §8(e).

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[2]In sharp contrast to the Agency's 1977 and 1978 actions to soliciting public comment on the proposed and final §8(e) Policy, EPA has unilaterally pronounced §8(e) substantive reporting criteria in the 1991 Section 8(e) Guide without public notice and comment, See 42 Fed Reg 45362 (9/9/77), "Notification of Substantial Risk under Section 8(e): Proposed Guidance".

[3]A comparison of the 1978 Statement of Interpretation and the 1992 "Reporting Guide" is a appended.

Throughout the CAP, EPA has mischaracterized the 1991 guidance as reflecting "longstanding" EPA policy concerning the standards by which toxicity information should be reviewed for purposes of §8(e) compliance. Regulatee recognizes that experience with the 1978 Statement of Interpretation may cause a review of its criteri. Regulatee supports and has no objection to the Agency's amending reporting criteria *provided that* such amendment is not applied to the regulated community in an unfair way. However, with the unilateral announcement of the CAP under the auspices of an OCM enforcement proceeding, EPA has wrought a terrific unfairness since much of the criteria EPA has espoused in the June 1991 Reporting Guide and in the Agency's April 2, 1992 amendment is new criteria which does not.exist in the 1978 Statement of Interpretation and Enforcement Policy.

The following examples of new criteria contained in the "Reporting Guide" that is not contained in the Statement of Interpretation follow:

- o even though EPA expressly disclaims each "status report" as being preliminary evaluations that should not be regarded as final EPA policy or intent[4], the "Reporting Guide" gives the "status reports" great weight as "sound and adequate basis" from which to determine mandatory reporting obligations. ("Guide" at page 20).
- o the "Reporting Guide" contains a matrix that establishes new numerical reporting "cutoff" concentrations for acute lethality information ("Guide" at p. 31). Neither this matrix nor the cutoff values therein are contained in the Statement of Interpretation. The regulated community was not made aware of these cutoff values prior to issuance of the "Reporting Guide" in June, 1991.
- othe "Reporting Guide" states new specific definitional criteria with which the Agency, for the first time, defines as 'distinguishable neurotoxicological effects'; such criteria/guidance not expressed in the 1978 Statement of Interpretation.[5];

- othe "Reporting Guide" provides new review/ reporting criteria for irritation and sensitization studies; such criteria not previously found in the 1978 Statement of Interpretation/Enforcement Policy.
- othe "Reporting Guide" publicizes certain EPA Q/A criteria issued to the Monsanto Co. in 1989 which are not in the Statement of Interpretation; have never been published in the Federal Register or distributed by the EPA to the Regulatee. Such Q/A establishes new reporting criteria not previously found in the 1978 Statement of Interpretation/Enforcement Policy .

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[4]The 'status reports' address the significance, if any, of particular information reported to the Agency, rather than stating EPA's interpretation of §8(e) reporting criteria. In the infrequent instances in which the status reports contain discussion of reportability, the analysis is invariably quite limited, without substantial supporting scientific or legal rationale.

[5] *See, e.g,* 10/2/91 letter from Du Pont to EPA regarding the definition of 'serious and prolonged effects' as this term may relate to transient anesthetic effects observed at lethal levels; 10/1/91 letter from the American Petroleum Institute to EPA regarding clarification of the Reporting Guide criteria.

In discharging its responsibilities, an administrative agency must give the regulated community fair and adequate warning to as what constitutes noncompliance for which penalties may be assessed.

> Among the myriad applications of the due process clause is the fundamental principle that statutes and regulations which purport to govern conduct must give an adequate warning of what they command or forbid.... Even a regulation which governs purely economic or commercial activities, if its violation can engender penalties, must be so framed as to provide a constitutionally adequate warning to those whose activities are governed.

Diebold, Inc. v. Marshall, 585 F.2d 1327, 1335-36 (D.C. Cir. 1978). *See also*, Rollins Environemntal Services (NJ) Inc. v. U.S. Environmental Protection Agency, 937 F. 2d 649 (D.C. Cir. 1991).

While neither the are rules, This principle has been applied to hold that agency 'clarification', such as the Statement of Interpretation, the "Reporting Guide" nor the April 1992 amendments will not applied retroactively.

> ...a federal court will not retroactively apply an unforeseeable interpretation of an administrative regulation to the detriment of a regulated party on the theory that the post hoc interpretation asserted by the Agency is generally consistent with the policies underlying the Agency's regulatory program, when the semantic meaning of the regulations, as previously drafted and construed by the appropriate agency, does not support the interpretation which that agency urges upon the court.

Standard Oil Co. v. Federal Energy Administration, 453 F. Supp. 203, 240 (N.D. Ohio 1978), aff'd sub nom. Standard Oil Co. v. Department of Energy, 596 F.2d 1029 (Em. App. 1978):

The 1978 Statement of Interpretation does not provide adequate notice of, and indeed conflicts with, the Agency's current position at §8(e) requires reporting of all 'positive' toxicological findings without regard to an assessment of their relevance to human health. In accordance with the statute, EPA's 1978 Statement of Interpretation requires the regulated community to use scientific judgment to evaluate the significance of toxicological findings and to determining whether they reasonably support a conclusion of a substantial risk. Part V of the Statement of Interpretation urges persons to consider "the fact or probability" of an effect's occurrence. Similarly, the 1978 Statement of Interpretation stresses that an animal study is reportable only when "it contains reliable evidence ascribing the effect to the chemical." 43 Fed Reg. at 11112. Moreover, EPA's Statement of Interpretation defines the substantiality of risk as a function of both the seriousness of the effect and the probability of its occurrence. 43 Fed Reg 11110 (1978). Earlier Agency interpretation also emphasized the "substantial" nature of a §8(e) determination. See 42 Fed Reg 45362, 45363

(1977). [Section 8(e) findings require "extraordinary exposure to a chemical substance...which critically imperil human health or the environment"].

The recently issued "Reporting Guide" and April 1992 Amendment guidance requires reporting beyond and inconsistent with that required by the Statement of Interpretation. Given the statute and the Statement of Interpretation's explicit focus on substantial human or environmental risk, whether a substance poses a "substantial risk" of injury requires the application of scientific judgment to the available data on a case-by-case basis.

If an overall weight-of-evidence analysis indicates that this classification is unwarranted, reporting should be unnecessary under §8(e) because the available data will not "reasonably support the conclusion" that the chemical presents a substantial risk of serious adverse consequences to human health.

Neither the legislative history of §8(e) nor the plain meaning of the statute support EPA's recent lowering of the reporting threshold that TSCA §8(e) was intended to be a sweeping information gathering mechanism. In introducing the new version of the toxic substances legislation, Representative Eckhart included for the record discussion of the specific changes from the version of H. R. 10318 reported by the Consumer Protection and Finance Subcommittee in December 1975. One of these changes was to modify the standard for reporting under §8(e). The standard in the House version was changed from "causes or contributes to an unreasonable risk" to "causes or significantly contributes to a substantial risk". This particular change was one of several made in TSCA §8 to avoid placing an undue burden on the regulated community. The final changes to focus the scope of Section 8(e) were made in the version reported by the Conference Committee.

The word "substantial" means "considerable in importance, value, degree, amount or extent". Therefore, as generally understood, a "substantial risk" is one which will affect a considerable number of people or portion of the environment, will cause serious injury and is based on reasonably sound scientific analysis or data. Support for the interpretation can be found in a similar provision in the Consumer Product Safety Act. Section 15 of the CPSA defines a "substantial product hazard" to be:

> "a product defect which because of the pattern of defect, the number of defective products distributed in commerce, the severity of the risk, or otherwise, creates a substantial risk of injury to the public."

Similarly, EPA has interpreted the word 'substantial' as a quantitative measurement. Thus, a 'substantial risk' is a risk that can be quantified, *See,* 56 Fed Reg 32292, 32297 (7/15/91). Finally, since information pertinent to the exposure of humans or the environment to chemical substances or mixtures may be obtained by EPA through Sections 8(a) and 8(d) regardless of the degree of potential risk, §8(e) has specialized function. Consequently, information subject to §8(e) reporting should be of a type which would lead a reasonable man to conclude that some type action was required immediately to prevent injury to health or the environment.

Attachment

Comparison:

Reporting triggers found in the 1978 "Statement of Interpretation/ Enforcement Policy",43 Fed Reg 11110 (3/16/78) and the June 1991 *Section 8(e) Guide.*

TEST TYPE	1978 POLICY CRITERIA EXIST?	New 1991 GUIDE CRITERIA EXIST?
ACUTE LETHALITY		
Oral	N}	Y}
Dermal	N}	Y}
Inhalation (Vapors)	}[6]	}[7]
aerosol	N}	Y}
dusts/ particles	N}	Y}
SKIN IRRITATION	N	Y[8]
SKIN SENSITIZATION (ANIMALS)	N	Y[9]
EYE IRRITATION	N	Y[10]
SUBCHRONIC (ORAL/DERMAL/INHALATION)	N	Y[11]
REPRODUCTION STUDY	N	Y[12]
DEVELOPMENTAL TOX	Y[13]	Y[14]

[6] 43 Fed Reg at 11114, comment 14:

"This policy statements directs the reporitng of specifiec effects when unknown to the Administrator. Many routine tests are based on a knowledge of toxicity associated with a chemicalL unknown effects occurring during such a range test may have to be reported if they are those of concern tot he Agency and if the information meets the criteria set forth in Parts V and VII."

[7] Guide at pp.22, 29-31.

[8] Guide at pp-34-36.

[9] Guide at pp-34-36.

[10] Guide at pp-34-36.

[11] Guide at pp-22; 36-37.

[12] Guide at pp-22

[13] 43 Fed Reg at 11112

"Birth Defects" listed.

[14] Guide at pp-22

NEUROTOXICITY	N	Y[15]
CARCINOGENICITY	Y[16]	Y[17]
MUTAGENICITY		
In Vitro	Y}[18]	Y} [19]
In Vivo	Y}	Y}
ENVIRONMENTAL		
Bioaccumulation	Y}	N
Bioconcentration	Y}[20]	N
Oct/water Part. Coeff.	Y}	N
Acute Fish	N	N
Acute Daphnia	N	N
Subchronic Fish	N	N
Subchronic Daphnia	N	N
Chronic Fish	N	N
AVIAN		
Acute	N	N
Reproductive	N	N
Reprodcutive	N	N

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[15] Guide at pp-23; 33-34.

[16] 43 Fed Reg at 11112
"Cancer" listed

[17] Guide at pp-21.

[18] 43 Fed Reg at 11112; 11115 at Comment 15
"Mutagenicity" listed/ *in vivo* vs *invitro* discussed; discussion of "Ames test".

[19] Guide at pp-23.

[20] 43 Fed Reg at 11112; 11115 at Comment 16.

(9)

CAS: 75-69-4; 75-71-8; 76-14-2; 75-00-3
Chem: trichlorofluoromethane; dichlorodifluoromethane; 1,2-dichlorotetrafluoroethane; ethyl chloride
Title: Cardiac Sensitizatin potential of propellant mixtures
Date: 12/19/72
Summary of Effect: cardiac sensitization

MEDICAL RESEARCH PROJECT - MR-1622

CARDIAC SENSITIZATION POTENTIAL OF PROPELLANT MIXTURES

INTRODUCTION

The ability of certain chemicals to produce cardiac sensitization in the mammalian heart has been studied at Haskell Laboratory for several years. This has been done by exposing healthy, male, beagle dogs to a fixed concentration of a single sensitizing agent in air and then challenging the animals with an injected dose of epinephrine. However, the interaction of two or more sensitizers, acting simultaneously on the heart, has received limited experimental attention. Since aerosol systems often contain two or more propellants in combination, it is important to know the effect of the resulting interaction on cardiac sensitization potential as compared to the individual action of each component.

In this study, the cardiac sensitization potential of two individual mixtures, each at two concentration levels in air, was determined using our standard cardiac sensitization test. A mixture of fluorocarbon 11 and flucrocarbon 12 (1:1 by volume) and a second mixture of fluorocarbon 12, fluorocarbon 114, and ethyl chloride (1:1:1 by volume) were tested and results compared with those of the individual components of each mixture.

METHODOLOGY

A. Materials

The materials studied are listed below and were obtained from Freon® Products Division, Organic Chemicals Department:

CARDIAC SENSITIZATION POTENTIAL OF PROPELLANT MIXTURES

Medical Research Project No. 1622

Haskell Laboratory Report No. 526-72

Report by: Henry J. Trochimowicz
Henry J. Trochimowicz

Linda S. Mullin
Linda S. Mullin

Approved by: Charles F. Reinhardt
Charles F. Reinhardt
Assistant Director

HJT/LSM/jtd
DATE: December 19, 1972
N.B. E0571 pp. 18, 22, 23, 25, 26
E0567 pp. 106-121, 124-129

Compound	Haskell Number
Trichlorofluoromethane (Freon® 11, F-11)	7667
Dichlorodifluoromethane (Freon® 12, F-12)	7668
1,2-Dichlorotetrafluoroethane (Freon® 114, F-114)	7507
Chloroethane (Ethyl Chloride, C_2H_5Cl)	7779

B. Procedure

In this experiment, the procedure used was the standard cardiac sensitization test which has been described previously (Haskell Laboratory Report No. 14-69). Dogs were exposed to test mixtures of (1) F-11 and F-12 and (2) F-12, F-114, and C_2H_5Cl at the concentrations shown in Table I. Twelve dogs per level were used. Each dog received a control injection of epinephrine (0.008 mg/kg) intravenously prior to exposure and a challenge injection (same dosage) after breathing the test mixture for five minutes. The animal then continued to breathe the mixture for five additional minutes following the challenge injection. An ECG was recorded continuously during each experimental run.

C. Generation and Administration of Vapor

1. Mixture of Fluorocarbon 11 and Fluorocarbon 12.

The desired concentrations in Table I were achieved by delivering a metered volume of F-11 and F-12, respectively, and diluting this mixture with a known amount of air. Fluorocarbon 12 was released as a gas from a pressurized cylinder, through a flow meter, into a metered airstream. Fluorocarbon 11, a liquid at room temperature, was then pumped (syringe drive) at a calculated rate into the F-12 and air mixture. The final mixture then passed through a heated copper delivery line and a heated 1-liter mixing chamber to the dog.

2. Mixture of Fluorocarbon 12, Fluorocarbon 114, and Ethyl Chloride.

All three materials are gases at room temperature and were generated from pressurized cylinders, through calibrated flow meters, and into a metered airstream resulting in the concentrations shown in Table I. The final mixture then passed through the unheated copper delivery line and mixing chamber to the dog.

D. Measurement of Vapor Concentration

A small portion of each test mixture was continuously withdrawn for chromatographic analysis at a point just before the mixture entered the dog mask with the use of a sampling pump. For the F-11-F-12 mixture, samples were analyzed every minute during exposure to each of the two test concentrations with the use of a Varian Aerograph 600D gas chromatograph equipped with a flame ionization detector and an automatic sampling valve. The column used was stainless steel, 5 feet in length with an outside diameter of 1/8 inch. The column material was 20% Si Oil on a packing material of 60/80 Chromasorb W. Nitrogen, which was the carrier gas, was set at 24 ml/min. The column temperature was 105°C; the hydrogen flow rate, 20.5 ml/min. The chromatographic separation of F-11 and F-12 is shown in Figure 1.

For the F-12-F-114-C_2H_5Cl mixture, samples were withdrawn and analyzed every two minutes by a Varian Aerograph Series 200 gas chromatograph employing a thermal conductivity detector. The column was stainless steel, 5 feet in length and 1/4 inch in diameter. The column material was Poropak T, 80/100 mesh. The filaments were set at 220 milliamps. Injector temperature was set at 100°C, column temperature at 158°C, and detector temperature at 188°C. Helium served as the carrier gas at a flow rate of

133 ml/min. The chromatographic separation of F-12, F-114, and C_2H_5Cl is shown in Figure 2.

RESULTS

The results of exposure to a mixture of F-11 and F-12, contrasted with previous Haskell Laboratory data on the individual components, are shown in Table II. A marked response indicates the development of multiple consecutive ventricular beats or ventricular fibrillation after a challenge injection of epinephrine. It is seen that no marked responses occurred when dogs were exposed to a mixture containing 0.1% F-11, 0.1% F-12, balance air; the same result (0 of 12 marked responses) was obtained with F-11 alone at 0.1% (V/V in air) and would be expected with 0.1% F-12 (V/V in air). However, the mixture containing 0.5% F-11, 0.5% F-12, balance air, did produce 3 of 12 (25%) marked responses in the test animals. Although previous test results are not available on F-12 at 0.5% (V/V in air), one would expect this concentration to produce 0 of 12 marked responses. Freon® 11 at 0.5% (V/V in air), on the other hand, had elicited 1 of 12 marked responses. To verify the preceding result on 0.5% F-11, it was decided to re-test this concentration level on our standard cardiac sensitization test using the same 12 dogs that gave 3 of 12 marked responses after exposure to the 1.0% mixture of F-11 and F-12 (0.5% of each, balance air). The results, shown in Table III, confirm our previous result in that 1 of 12 dogs were sensitized to exogenous epinephrine at an inspired concentration of 0.5% F-11.

For the second test mixture (F-12, F-114, C_2H_5Cl), cardiac sensitization results contrasted with results on individual components of that mixture are tabulated in Table IV. It is seen that no marked responses

(0 of 12) were elicited in dogs exposed to a 2.5% mixture (i.e., 0.83% of each, balance air). Although F-12, F-114, and C_2H_5Cl were not tested individually at 0.83% (V/V in air), the expected result would be 0 of 12 marked responses, also. However, when dogs were exposed to the 5.0% mixture (F-12, F-114, and C_2H_5Cl at 1.67% each, balance air), the result was 4 of 12 marked responses. Comparing these results with those of the individual mixture components, it is seen that, at 2.5% (V/V in air), a test concentration common to all three compounds, F-114 and C_2H_5Cl respectively, elicited 1 of 12 (8.3%) marked responses while F-12 produced no marked responses in 12 dogs.

DISCUSSION

From the results shown in Table II on a 1.0% mixture of F-11 and F-12 (0.5% of each, balance air) and in Table IV on a 5.0% mixture of F-12, F-114, and C_2H_5Cl (1.67% of each, balance air), it appears that the resulting interaction of test components may be more than additive when compared to cardiac sensitization results on individual components. However, it is important to note that this observation is based on only one concentration level (i.e., one "effect level") from each mixture. Thus, it is evident that additional work is needed in order to elucidate the nature of the interaction of two or more compounds which may be acting simultaneously on the heart. For any mixture of interest, a dose-response curve for each mixture component is a necessary prerequisite. This requires testing at three or four concentration levels for each compound. The components of the two mixtures in this investigation do not meet this requirement. After establishing individual dose-response curves,

prediction can then be made on the resulting interaction of two or more compounds and verified by testing the mixture itself at three concentration levels.

In the light of preliminary results from this investigation, the further development of a predictive model for certain fluorocarbon combinations appears promising and can be done with a minimal amount of additional testing. Using the data generated on F-11 and F-12 alone and in combination, a sample predictive model for this mixture is shown in Figure 3. It is seen that for any combination of F-11 and F-12 in air within a given range, an estimation of cardiac sensitzation potential can easily be calculated. However, an accurate prediction of cardiac sensitization potential would require additional data points. For example, F-11 and F-12 would have to be tested, respectively, at two more concentration levels (V/V in air), and the mixture of F-11 and F-12 would also have to be tested at two additional levels. Thus, an accurate predictive model for this particular mixture could be completed at a reasonable cost.

HJT/jtd
1-30-73

TABLE I

EXPOSURE PROFILE

Test Mixture		Nominal Concentration	Measured Concentration*
A. F-11 + F-12			
1)	F-11	0.1%	0.10 ± 0.0056%
	F-12	0.1%	0.10 ± 0.0046%
2)	F-11	0.5%	0.51 ± 0.0079%
	F-12	0.5%	0.50 ± 0.0075%
B. F-12 + F-114 + C_2H_5Cl			
1)	F-12	0.83%	0.83 ± 0.014%
	F-114	0.83%	0.86 ± 0.017%
	C_2H_5Cl	0.83%	0.87 ± 0.020%
2)	F-12	1.67%	1.64 ± 0.036%
	F-114	1.67%	1.65 ± 0.022%
	C_2H_5Cl	1.67%	1.66 ± 0.033%

*Average and standard deviation for 12 dog exposures per mixture level.

TABLE II

RESULTS OF CARDIAC SENSITIZATION TESTING:
MIXTURE (F-11 AND F-12) VS. INDIVIDUAL COMPONENT*

Test Compound	Concentration (% V/V)	Duration of Exposure (Min.)	Number of Dog Exposures	Number of Marked Responses	Percent Marked Responses	Comments
Mixture of F-11 & F-12	0.2(0.1 Ea.)	5	12	0	0	
	1.0(0.5 Ea.)	5	12	3	25.0	
Freon® 11	0.1	5	12	0	0	
	0.5	5	12	1(1)**	8.3	
	1.0	5	12	5(3)	41.7	
Freon® 12	2.5	5	12	0	0	
	5.0	5	12	5(1)	41.7	

* Individual data on F-11 and F-12 from C. F. Reinhardt et al., Arch. Environ. Hlth. 22: 265, 1971.

** Numbers in parentheses indicate number of cases of ventricular fibrillation and cardiac arrest included in marked responses.

TABLE III

RESULTS OF CARDIAC SENSITIZATION TESTING ON FREON® 11:
A COMPARISON WITH PREVIOUSLY REPORTED DATA

Test Compound	Concentration (% V/V)	Duration of Exposure (Min.)	Number of Dog Exposures	Number of Marked Responses	Percent Marked Responses	Comments
Freon® 11	0.50	5	12	1(1)*	8.3	A result previously reported by Reinhardt et al.(1971)
Freon® 11	0.50	5	12	1	8.3	A result from the present study

* Number in parentheses indicates number of cases of ventricular fibrillation and cardiac arrest included in marked responses.

TABLE IV

RESULTS OF CARDIAC SENSITIZATION TESTING:
MIXTURE (F-12, F-114, & C_2H_5Cl) VS. INDIVIDUAL COMPONENT*

Test Compound	Concentration (% V/V)	Duration of Exposure (Min.)	Number of Dog Exposures	Number of Marked Responses	Percent Marked Responses	Comments
Mixture of F-12, F-114 & C_2H_5Cl	2.5(0.83% Ea.)	5	12	0	0	
	5.0(1.67% Ea.)	5	12	4	33.3	
Freon® 12	2.5	5	12	0	0	
	5.0	5	12	5(1)**	41.7	
Freon® 114	2.5	5	12	1	8.3	
	5.0	5	12	7(2)	58.3	
Ethyl Chloride	1.0	5	12	0	0	
	2.5	5	12	1	8.3	Dog who reacted at 2.5% was also tested at 2% and again had a ma response.
	4.0	5	6	2	33.3	
	5.0	5	2	2	100.0	

* Individual data on F-12 and F-114 from C. F. Reinhardt et al., Arch. Environ. Hlth. 22: 265, 1971; C_2H_5Cl from HL Report 395-71.

** Number in parentheses indicate number of cases of ventricular fibrillation and cardiac arrest included in marked res

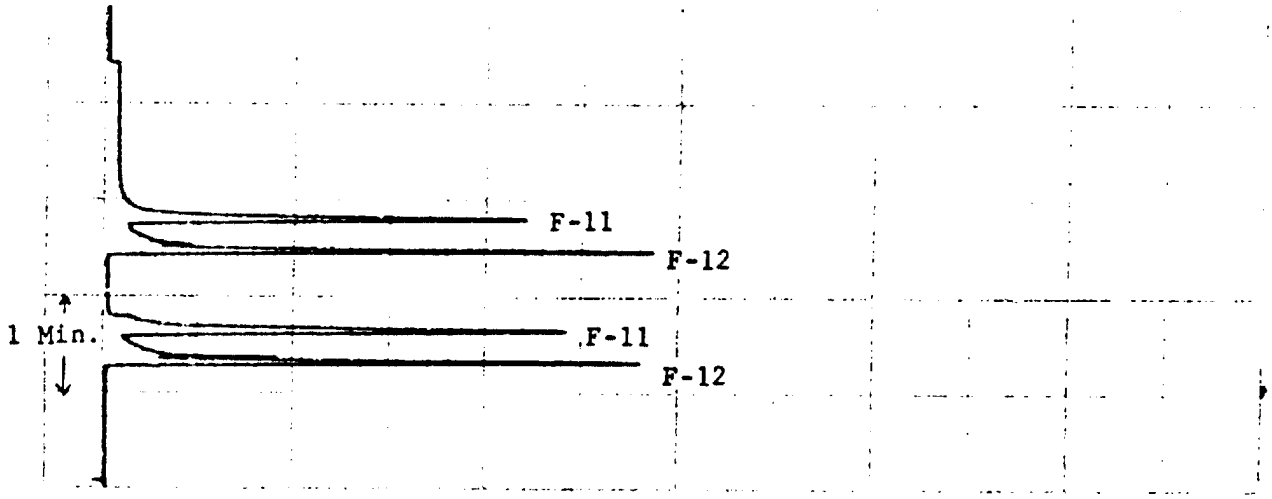


Figure 1. Chromatographic Separation of Freon® 11 and Freon® 12.

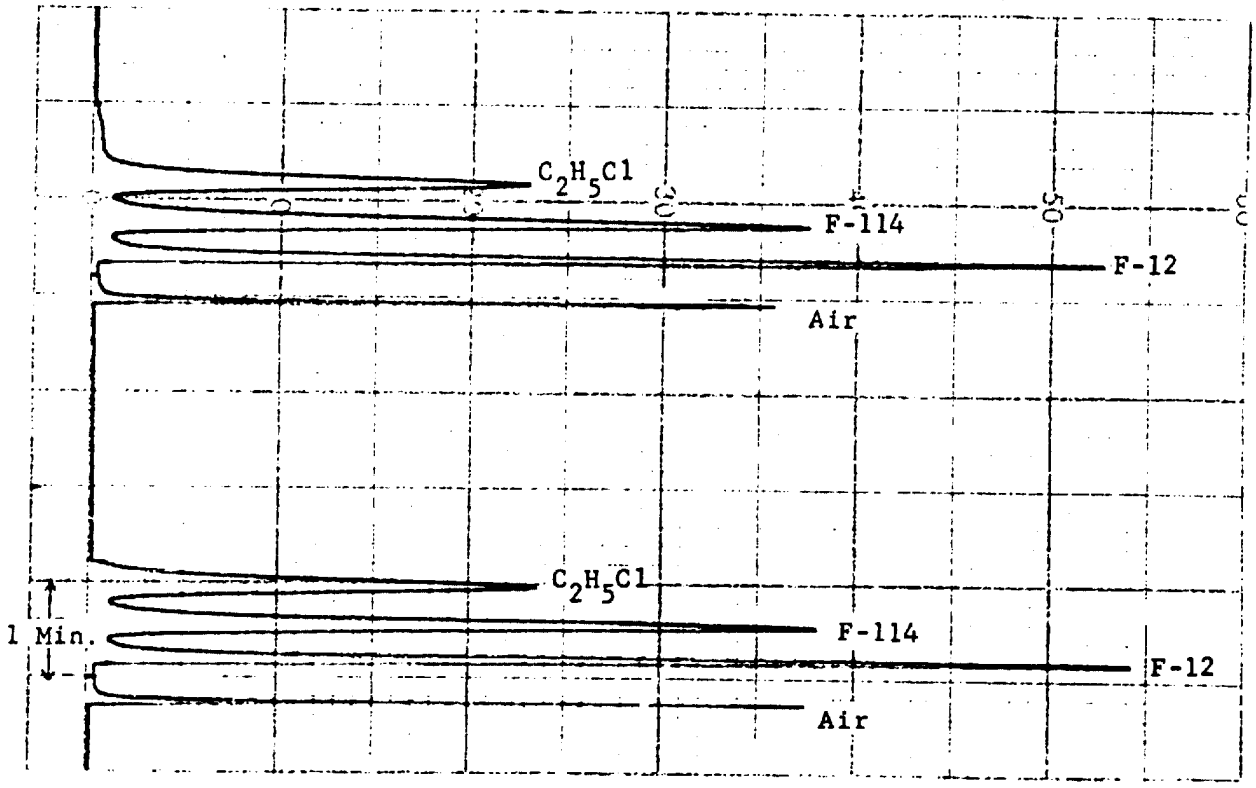
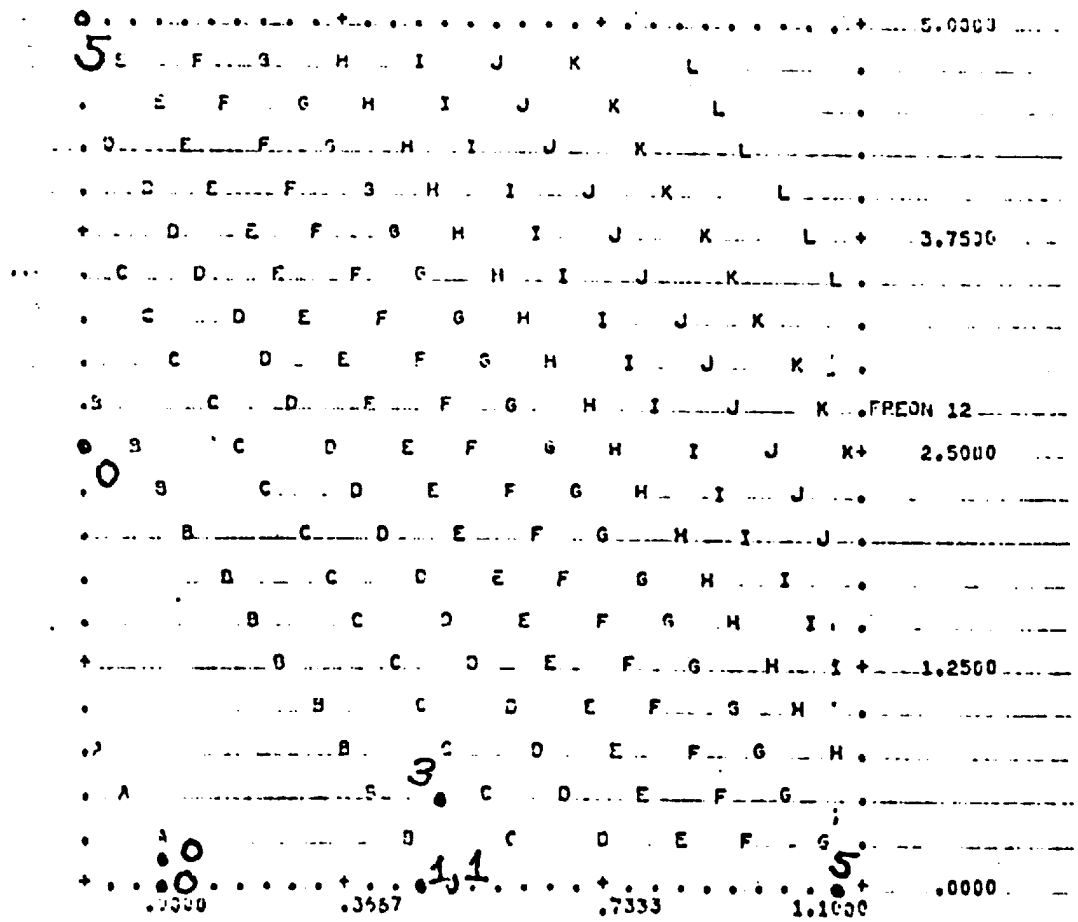


Figure 2. Chromatographic Separation of Freon® 12, Freon® 114, and Ethyl Chloride.

Figure 3. Effect of a Mixture of Freon® 11 and Freon® 12 on Cardiac Sensitization*



CODE	NO. MARKED RESPONSES
A	0
B	1
C	2
D	3
E	4
F	5
G	6
H	7
I	8
J	9
K	10
L	11

DATA POINTS
(12 dogs/conc. level)

F-11 (%)	F-12 (%)	NO. MARKED RESPONSES
.11	0	0
.48	0	1
1.08	0	5
0	2.5	0
0	5.0	5
.5	.5	3
.5	0	1
.1	.1	0

*Model developed by Dr. R. D. Snee, Louviers.

Triage of 8(e) Submissions

Date sent to triage: _____ NON-CAP (CAP)

Submission number: 13162A TSCA Inventory: (Y) N D

Study type (circle appropriate):

Group 1 - Dick Clements (1 copy total)

ECO AQUATO

Group 2 - Ernie Falke (1 copy total)

ATOX SBTOX (SEN) w/NEUR

Group 3 - Elizabeth Margosches (1 copy each)

STOX CTOX EPI RTOX GTOX

STOX/ONCO CTOX/ONCO IMMUNO CYTO NEUR

Other (FATE, EXPO, MET, etc.): _____

Notes:

THIS IS THE ORIGINAL 8(e) SUBMISSION; PLEASE REFILE AFTER TRIAGE DATABASE ENTRY

For Contractor Use Only

entire document: (0) 1 2 **pages** 1,9 **pages** _____

Notes:

Contractor reviewer : JW **Date:** 1/24/96

CI:CATS\TRIAGE TRACKING DBASE ENTRY FORM

CECATS DATA:
Submission # (EPA): 1192-13162 SEQ: A

TYPE: (INT) SUPP FLWP

SUBMITTER NAME: E. I. Dupont de Nemours and Company

INFORMATION REQUESTED: FLWP DATE:
0301 NO INFO REQUESTED
0302 INFO REQUESTED (TECH)
0303 INFO REQUESTED (VOL ACTIONS)
0304 INFO REQUESTED (REPORTING RATIONALE)

DISPOSITION:
(0530) REFER TO CHEMICAL SCREENING
(0570) CAP NOTICE

VOLUNTARY ACTIONS:
(0481) NO ACTION REPORTED
0482 STUDIES PLANNED/ONGOING
0483 NOTIFICATION OF WORKER EXPOSURE
0484 LABELMODS CHANGES
0485 PROCESS/MAINT MOD CHANGES
0486 APPLIUSE DISCONTINUED
0487 PRODUCTION DISCONTINUED
0488 CONFIDENTIAL

SUB. DATE: 10/18/92 OTS DATE: 11/02/92 CSRAD DATE: 04/24/95

CHEMICAL NAME:	CAS#
Freon 11	75-69-4
Freon 12	75-71-8
Freon 114	76-14-2
	75-00-3

INFORMATION TYPE:		P F C	INFORMATION TYPE:		P F C	INFORMATION TYPE:		P F C
0201	ONCO (HUMAN)	01 02 04	0216	EPICLIN	01 02 04	0801	BIOLUMO (ANIMAL)	01 02 04
0202	ONCO (ANIMAL)	01 02 04	0217	HUMAN EXPOS (PROD CONTAM)	01 02 04	0802	BIOLUMO (HUMAN)	01 02 04
0203	CELL TRANS (IN VITRO)	01 02 04	0218	HUMAN EXPOS (ACCIDENTAL)	01 02 04	0803	CHEMPHYS PROP	01 02 04
0204	MUTA (IN VITRO)	01 02 04	0219	HUMAN EXPOS (MONITORING)	01 02 04	0804	CLASTO (IN VITRO)	01 02 04
0205	MUTA (IN VIVO)	01 02 04	0220	ECOAQUA TOX	01 02 04	0805	CLASTO (ANIMAL)	01 02 04
0206	REPRO/TERATO (HUMAN)	01 02 04	0221	ENV. OCCCORE/FATE	01 02 04	0806	CLASTO (HUMAN)	01 02 04
0207	REPRO/TERATO (ANIMAL)	01 02 04	0222	EMER INCI OF ENV CONTAM	01 02 04	0807	DNA DAMAGE/REPAIR	01 02 04
0208	NEURO (HUMAN)	01 02 04	0223	RESPONSE REQUST DELAY	01 02 04	(0808)	PRODUSE/PROC	01 02 04
0209	NEURO (ANIMAL)	01 02 04	(0224)	PROD/COMP/CHEM ID	01 02 04	0851	MEDS	01 02 04
0210	ACUTE TOX. (HUMAN)	01 02 04	0225	REPORTING RATIONALE	01 02 04	0899	OTHER	01 02 04
0211	CHR. TOX. (HUMAN)	01 02 04	0226	CONFIDENTIAL	01 02 04			
0212	ACUTE TOX. (ANIMAL)	01 02 04	0227	ALLERG (HUMAN)	01 02 04			
0213	SUB ACUTE TOX (ANIMAL)	01 02 04	(0228)	ALLERG (ANIMAL)	01 02 04			
0214	SUB CHRONIC TOX (ANIMAL)	01 02 04	0229	METABPHARMACO (ANIMAL)	01 02 04			
0215	CHRONIC TOX (ANIMAL)	01 02 04	0240	METABPHARMACO (HUMAN)	01 02 04			

TRIAGE REVIEW	NON-CBI INVENTORY	SCREENING REVIEW	SPECIES	TOXICOLOGICAL CONCERN:	USE:	PRODUCTION:
	(YES)	YES (DROP/REFER)	DOG	(LOW) Cardiac sensit.	propellant	
CAS SR	NO	NO (CONTINUE)		MED		
	UNKNOWN	REFER		HIGH		

COMMENTS:

13162A

L

Freon 11/Freon 12: Cardiac sensitization in dogs is of low concern. Beagle dogs were challenged with epinephrine during 5-minute exposures to 2,000 and 10,000 ppm of the test mixture. Multiple consecutive ventricular beats or ventricular fibrillation occurred in 0/12 dogs at 2,000 ppm and 3/12 dogs at 10,000 ppm.

L

Freon 11: Cardiac sensitization in dogs is of low concern. Beagle dogs were challenged with epinephrine during a 5-minute exposure to 5,000 ppm of the test substance. Multiple consecutive ventricular beats or ventricular fibrillation occurred in 1/12 dogs at 5,000 ppm.

L

Freon 12/Freon 114/ethyl chloride: Cardiac sensitization in dogs is of low concern. Beagle dogs were challenged with epinephrine during 5-minute exposures to 25,000 and 50,000 ppm of the test mixture. Multiple consecutive ventricular beats or ventricular fibrillation occurred in 0/12 dogs at 25,000 ppm and 4/12 dogs at 50,000 ppm.